Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

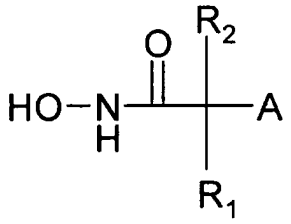
1. (Canceled)

2. (Currently Amended) A method of treating cancer in a subject in need of such treatment which comprises:

~~radiotherapy,~~

~~or cytotoxic therapy~~ a chemotherapy drug in combination with heat shock,

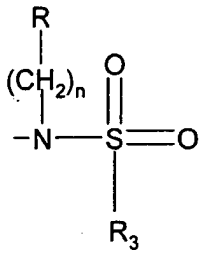
and further comprises administering to the subject an effective amount of a matrix metalloproteinase inhibitor of the formula I



(I)

(i) wherein

A represents substituent of formula II or III;



Formula II

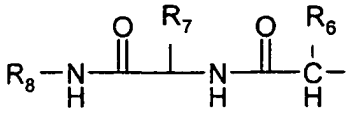
wherein

R represents hydrogen, lower alkyl, aryl-lower alkyl, aryl, mono- or poly-halo-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, (oxa or thia)-cycloalkyl, [(oxa or thia)-cycloalkyl]-lower alkyl, hydroxy-lower alkyl, acyloxy-lower alkyl, lower alkoxy-lower alkyl, lower alkyl-(thio, sulfinyl or sulfonyl)-lower alkyl, (amino, mono- or di-lower alkylamino)-lower alkyl, acylamino-lower alkyl, (N-lower alkyl-piperazino or N-aryl- lower alkylpiperazino)-lower alkyl, or (morpholino, thiomorpholino, piperidino, pyrrolidino, piperidyl or N-lower alkylpiperidyl)-lower alkyl;

R_3 represents aryl that may be unsubstituted or substituted by R_4 and R_5;

R_4 or R_5 represents independently hydrogen, lower alkyl, lower alkoxy, halogen, hydroxy, acyloxy, lower alkoxy-lower alkoxy, trifluromethyl or cyano, oxy-C2-C3-alkylene, 1- or 2-napthyl; or R_4 and R_5 together on adjacent carbon atoms represent lower alkylenedioxy;

n represents an integer from 1 to 5;



Formula III

wherein

R_6 is C_{3-12} alkyl, C_{3-12} alkenyl, C_{3-7}(optionally hydroxy-, C_{1-6} alkoxy-, amino-, or C_{1-6} alkylamino-substituted) cycloalkyl, C_{5-14} aryl, or C_{5-14} aryl(C_{1-6} alkyl), wherein aryl groups are optionally substituted by hydroxy-, C_{1-6} alkyl-, C_{1-6} alkoxy-, amino-, halo- or cyano-;

R_7 is C_{1-10} (optionally hydroxy- or C_{1-6}alkoxy- amino-, C_{1-6} alkylamino-, thiol-, C_{1-6} alkylmercapto- or protected hydroxy-, amino- or thiol- substituted) alkyl, C_{6-14} (optionally hydroxy-, C_{6-14}aryloxy-, or C_{1-6}alkoxy-, amino-, C_{1-6} alkylamino-, halo-, or cyano- substituted)aryl, or indolylmethyl;

R_8 is methyl, pyridyl, or a substituent of formula X-Y- wherein X is morpholino, pyridyl or aryl, and Y is C_{1-12}alkylene in which up to four of the methylene (-CH_2-) units are optionally replaced with -CO-, -NH-, -SO_2- or -O-;

R_1 is hydrogen, lower alkyl, aryl, aryl-lower alkyl, mono- or poly-halo-lower alkyl, cycloalkyl, cycloalkyl-lower alkyl, cycloalkyl-cycloalkyl, aryl-lower alkyl-lower cycloalkyl, lower alkyl-cycloalkyl, lower alkoxy-lower alkyl-cycloalkyl, aryl-cycloalkyl, cycloalkyl-lower alkyl-cycloalkyl, halo-lower alkyl-cycloalkyl, hydroxy-lower alkyl, acyloxy-lower alkyl, lower alkoxy-lower alkyl, aryl-lower alkoxy-lower alkyl, lower alkyl-(thio, sulfinyl or sulfonyl)-lower alkyl, (amino, mono- or di-lower alkylamino)-lower alkyl, (N-lower alkyl-piperazino or N-aryl-lower alkylpiperazino)-lower alkyl, (morpholono, thiomorpholino, piperidino, pyrrolidino, piperidyl or N-lower alkylpiperidyl)-lower alkyl, acylamino-lower alkyl, piperidyl, N-lower alkylpiperidyl or a substituent of formula IV

D-(O-(CR_9H)$_z$)$_m$-O-CH_2- Formula IV

wherein

z is 1, 2, 3 or 4;

m is 0, 1, 2 or 3;

each R_9 is

independently H, C_{1-10} (optionally hydroxy-, C_{1-6} alkoxy-, amino-, C_{1-6} alkylamino-, thiol-, C_{1-6} alkylmercapto- or protected hydroxy, amino or thiol substituted) alkyl, C_{2-6} alkenyl, C_{6-14}(optionally hydroxy-, C_{1-6} alkoxy-, amino-, C_{1-6} alkylamino-, halo- or cyano- substituted) aryl, or C_{6-14} (aryl) C_{1-6}alkyl;

D is hydrogen, C_{1-10} alkyl, C_{6-14} aryl, C_{6-14} aryl(C_{1-6} alkyl), (C_{6-14} aryl)carbonyl, or (C_{1-10} alkyl)carbonyl;

R_2 is hydrogen or lower alkyl,

(ii) or wherein

R (of formula II under (a)) and R_1 together with the chain to which they are attached from a 1,2,3,4-tetrahydro-isoquinoline, piperidine, oxazolidine, thiazolidine or pyrrolidine ring, each unsubstituted or substituted by lower alkyl; and

R_3 and R_2 have meaning as defined under (i);

(iii) or wherein

R_1 and R_2 together with the carbon atom to which they are attached form a ring system selected from lowercycloalkane which is unsubstituted or substituted by lower alkyl' oxa-cyclohexane, thia-cyclohexane, indane, tetralin, piperidine or piperidine substituted on nitrogen by acyl, lower alkyl, aryl-lower alkyl, (carboxy, esterified or amidated carboxy)-lower alkyl or by lower alkylsulfonyl; and

R_3 and R meaning as defined under (i);

~~or a pharmaceutically acceptable prodrug derivative thereof;~~ or a pharmaceutically acceptable salt thereof.

3. (Canceled)

4. (Canceled)

5. (Currently Amended) A package comprising a matrix metalloproteinase inhibitor of formula I of claim 2 (or pharmaceutically acceptable salt ~~or prodrug ester~~ thereof) together with instructions for use in combination with

~~a) radiotherapy, or~~

~~b)~~ heat shock and ~~cytotoxic therapy~~ a chemotherapy drug in the treatment of tumor.

6. (canceled)

7. (Canceled)

8. (Currently Amended) A method according to claim ~~1~~ 2, in which the matrix metalloproteinase inhibitor is N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl) amino] -3-

methyl –butaneamide hydrochloride) monohydrate, ~~or a pharmaceutically acceptable prodrug derivative thereof,~~ or a pharmaceutically acceptable salt thereof.

9. (Currently Amended) A method according to claim ~~1~~ 2 in which the matrix metalloproteinase inhibitor, or a pharmacologically acceptable salt ~~or prodrug ester~~, is in the form of a enteral composition.

10. (Canceled)